

**Appl. No.** : **09/804,457**  
**Filed** : **March 12, 2001**

## **REMARKS**

### **Pending Claims**

Claims 1-8, 10-29, 49 and 50 remain pending in the application. Claims 1 and 21 have been amended to correct potential confusion with the language. These amendments do not constitute new matter.

### **Rejections under § 112 ¶ 1**

The Examiner rejected Claims 1-5 and 7-8 under 35 U.S.C. § 112 ¶ 1 as being unpatentable. The Examiner stated that “because the specification [of the present application] while being enabling for a method claimed where the field strength is 0.2% of the mean, does not reasonably provide enablement for a method claimed where the field strength is greater than 0.2% of the mean. . . . [T]he specification teaches that [an] electric field strength [] greater than 0.2% of the mean is enabled [], whereas the electric field of 10% of the mean is not acceptable.” More specifically, the Examiner states that “the specification [of the instant application] teaches that the electric field strength [] greater than 0.2% is enabled (page 97 of the specification) whereas the electric field of 10% [or greater] of the mean is not acceptable (page 96, line 10 of the specification.”

Applicants agree the specification teaches producing a variation in electric field greater than 10% from a mean intensity (in particular where the standard deviation of the field strength is 15% of the mean in the total area of observation as illustrated on page 96 of the specification) is not ideal. Nevertheless, the specification enables a method “producing a limited spatial variation in intensity in [an] electric field in [an] area of observation of within ±10% from a mean intensity in that area.” (Emphasis added) See, e.g., Example 1 page 95 (“the electric filed remains within ±10% of the mean field in the area of observation[, which] geometry satisfies the stated requirements for field uniformity for use in the present invention”), Example 3 pages 96-97 (“the electric filed remains within ±1% of the mean field in the area of observation[, which] geometry greatly improves the field uniformity”), Example 4 page 97 (“the electric filed remains within ±1% of the mean field in the area of observation[, which] geometry greatly improves the field uniformity”), Example 5 page 98 (“the difference between the maximum and minimum fields is 1.2% of the mean[, which] geometry greatly improves the field uniformity”) and Figures

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7A, 8A, 8B and 8C. Applicants thus argue that Claim 1 is enabled by the disclosure provided in the specification and request withdrawal of the Examiner's rejection of Claim 1 (and the claims that depend therefrom) for lack of enablement.

### **Provisional Double Patenting Rejections**

The Examiner has provisionally rejected Claims 1-8, 10-29, 49 and 50 on the ground of nonstatutory obviousness-type double patenting in light of Claims 1-6 of co-pending application no. 10/620,312 ("the '312 application"). Applicants note that the '312 application has not issued as a patent yet. Thus, this provisional rejection will be addressed in the present application if and when Claims 1-6 of the '312 application are allowed.

### **Rejection of Claims 1-8, 10-29, 49 and 50 under § 102(b)**

The Examiner has rejected Claims 1-8, 10-29, 49 and 50 under 35 U.S.C. § 102(b) as anticipated by Sinha et al. (1995) (hereinafter "Sinha"). As discussed in the telephonic interview of April 12, 2007, however, Sinha does not anticipate Claims 1-8, 10-29, 49 and 50. "A claim is anticipated [under § 102(b)] only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 (quoting *Verdegall Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987)).

Sinha does not disclose all of the elements of Claim 1. Claim 1 recites "[a] method of testing the effect of a candidate compound on the transmembrane potential of one or more biological cells comprising exposing one or more cells comprising at least one voltage regulated ion channel to said compound, repetitively exposing said one or more cells to a series of two or more electric fields so as to effect a change in transmembrane potential of said one or more cells without using a patch clamp, wherein said transmembrane potential changes predominantly in a single direction away from a starting transmembrane potential over the course of said series of electric fields due to a continuing and additive accumulation of charge in said cell over the course of said series of electric fields; and monitoring, without using a patch clamp, changes in the transmembrane potential of said one or more cells to test the effect of said compound on said one or more biological cells."

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One example of an embodiment of Claim 1 is found in Figure 4 of the present application. Electric fields (E) are pulsed causing a transmembrane current flow ( $I_{Na}$ ) and a step wise accumulation of charge in the cell ( $V_m$ ). Sinha discloses stimulating hippocampal cells with pulsed electric field potential. See e.g., Figure 4 and pages 55-56 of Sinha. In Figure 4 the time course of the optical signal (the VSD trace) is the same as that of the membrane potential. As shown in Figure 4B, however, the pulses (about 50 msec apart) do not accumulate charge in the cell over the course of the series of electric fields. Figure 4B illustrates a spike in potential charge followed by a rapid decay preceding a second pulse. Figures 5B and 6B of Sinha each illustrate a single pulse. In Figure 5B, the applied field potential (pulse) leads to a jump in the VSD that completely decays without application of any second pulse. Likewise, Figure 6 illustrates an application of an electric field potential that causes a jump in the VSD that thereafter decays. Nowhere does Sinha disclose a repetitive application of electric fields that “effect a change in transmembrane potential . . . predominantly in a single direction away from a starting transmembrane potential over the course of said series of electric fields due to a continuing and additive accumulation of charge in said cell over the course of said series of electric fields.” In fact, prior to the disclosure of the present application it was unknown in the art that a repetitive application of a series of electric pulses could effect a change in transmembrane potential due to a continuing and additive accumulation of charge in said cell over the course of said series of electric fields.” Applicants thus respectfully request that the Examiner’s rejection of Claim1 and the claims dependent therefrom be withdrawn.

Similarly, amended Claim 21 is not anticipated by Sinha. Amended Claim 21 recites a “method of assaying the effect of a compound against a target voltage regulated ion channel, wherein said effect is manifested by transmembrane potential changes comprising . . . repetitively exposing [a] population of cells to a series of two or more electric fields so as to effect a change in transmembrane potential of said population of cells, wherein said transmembrane potential changes predominantly in one direction away from a starting transmembrane potential over the course of said series of electric fields due to a continuing and additive accumulation of charge in said population of cells over the course of said series of electric fields.” As noted above, Sinha does not disclose or teach “repetitively exposing [a] population of cells to a series of two or more electric fields so as to effect a change in transmembrane potential of said population of cells,

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wherein said transmembrane potential changes predominantly in one direction away from a starting transmembrane potential over the course of said series of electric fields due to a continuing and additive accumulation of charge in said population of cells over the course of said series of electric fields.” Further, as described above, Sinha teaches stimulating hippocampal cells with pulsed electric field potentials producing transmembrane potential changes that rapidly decay after each pulse. Because Sinha does not teach or suggest each and every element of amended Claim 21, it does not anticipate amended Claim 21. Applicants thus respectfully request that the Examiners rejection of amended Claim 21 and the claims dependent therefrom be reconsidered and withdrawn.

### **CONCLUSION**

The Applicants have endeavored to address all of the Examiner’s concerns as expressed in the outstanding Office Action and also to reiterate the arguments presented during the telephonic interview of April 12, 2007. Accordingly, arguments in support of the patentability of the pending claim set are presented above. In light of these remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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